

Remarks

By the foregoing amendments, claims 53-88 have been canceled without prejudice or disclaimer, claims 26, 30 and 52 have been amended, and new claims 89-99 are sought to be entered. The amendment to claim 52 is sought to correct a minor typographical error in this claim, and therefore adds no new matter. Support for the remaining amendments to the claims may be found throughout the specification. Specifically, support for the amendments to claim 26 may be found at pages 36-45 of the specification; support for new claims 89 and 90 may be found at pages 36-38 and 41-45 of the specification and throughout the Examples, particularly at pages 75-87; and support for new claims 91-99 may be found in the specification at pages 38-41. Accordingly, the present amendments do not add new matter, and their entry is respectfully requested. Upon entry of the foregoing amendments, claims 26, 28-35, 52 and 89-99 are pending in the application, with claim 26 being the sole independent claim.

Applicants also wish to provide the following remarks concerning the Office Action dated May 22, 2000 (Paper No. 17).

I. Summary of the Interview

Applicants wish to thank the Examiner for the time taken to discuss the present application, and the Office Action dated May 22, 2000, with Applicants' undersigned representative during a personal interview held on October 12, 2000. During this interview, the cited art was discussed, as were several possible amendments to the claims and the applicability of 35 U.S.C. § 103(c) to certain art cited in the Office Action.

II. *Summary of the Office Action*

In the Office Action dated May 22, 2000, the Examiner made or maintained three rejections of the claims, and issued a restriction requirement/constructive election. Applicants offer the following remarks concerning each of these elements of the Office Action.

III. *The Restriction Requirement/Constructive Election*

In the Office Action at page 2, the Examiner has withdrawn claims 53-88 from consideration as being directed to a non-elected invention, contending that these claims are drawn to an invention that is independent of or distinct from the invention originally claimed and prosecuted in the present application. Applicants respectfully disagree with this contention. However, to expedite prosecution and allowance of the present application, claims 53-88 have now been canceled without prejudice or disclaimer by the foregoing amendments. As noted above, Applicants reserve the right to prosecute these claims in one or more continuation and/or divisional applications of the present application.

IV. *The Rejection Under 35 U.S.C. § 102(b) Over Bebee*

In the Office Action at page 3, first paragraph, the Examiner has maintained the rejection of claims 26-29 and 31-35, and has newly rejected claim 52, under 35 U.S.C. § 102(b) as being anticipated by Bebee (U.S. Patent No. 5,434,066; Doc. No. AB1, of record; hereinafter “Bebee”), for reasons set forth in the Office Action dated June 24, 1999 (Paper No. 8). Applicants respectfully traverse this rejection.

In making this rejection, the Examiner contended that:

Bebee *et al.* teach cloning of nucleic acids (DNA) by taking advantage of the Cre recombinase system. They teach the

sequences for the specific lox P sites recognized by the Cre enzyme (see for example column 5). They also teach PCR primers #790 and #791 which include the LoxP recombination sites and the amplification of a kanamycin resistance gene from a plasmid with said primers. They teach that as a result of PCR, a “cassette” or fragment comprising the kanamycin resistance gene flanked by loxP sites is obtained (see for example, columns 11 and 12). They further teach that this product (cassette) was ligated into another construct, indicating that as a result of PCR amplification, a double-stranded product was obtained.

Paper No. 8 at page 3, lines 1-8. Applicants offer the following remarks regarding this rejection.

As the Examiner has noted, the disclosure of Bebee is limited to use of the Cre/loxP system. In contrast, claim 26 as currently presented (and hence the remaining claims that depend therefrom) specifically excludes *lox* recombination sites from the scope of the invention as presently claimed. Under 35 U.S.C. § 102, a claim can only be anticipated if every element in the claim is expressly or inherently disclosed in a single prior art reference. *See Kalman v. Kimberly Clark Corp.*, 713 F.2d 760, 771 (Fed. Cir. 1983), *cert. denied*, 465 U.S. 1026 (1984). Since Bebee does not disclose any recombination sites other than *lox*, it fails to expressly or inherently disclose at least one element of claim 26 as currently presented. Hence, Bebee cannot and does not anticipate the presently claimed invention.

V. The Rejection Under 35 U.S.C. § 103(a) Over Kilby, Snaith or Hartley in View of Ausubel, Padgett or Grose

In the Office Action at page 3, paragraph 2, the Examiner has maintained the rejection of claims 26-29 and 31-35, and has newly rejected claim 52, under 35 U.S.C. § 103(a) as being unpatentable over Kilby *et al.* (Doc. No. AT10, of record; hereinafter “Kilby”), Snaith *et al.* (Doc. No. AR21, of record; hereinafter “Snaith”) or Hartley *et al.* (Doc. No. AG1, of record; hereinafter “Hartley”), in view of Ausubel *et al.* (Doc. “W” listed on the Form PTO-892 attached

to Paper No. 8; hereinafter “Ausubel”) and further in view of Padgett *et al.* (Doc. “X” listed on the Form PTO-892 attached to Paper No. 8; hereinafter “Padgett”) or Grose *et al.* (Doc. “C” listed on the Form PTO-892 attached to Paper No. 8; hereinafter “Grose”), for reasons set forth in Paper No. 8. Applicants respectfully traverse this rejection.

As a first matter, Applicants note that Hartley is assigned to the same assignee as is the present application, and names two common inventors. However, Applicants have not claimed priority in the present application to Hartley. Hence, Applicants presume that the basis for citing Hartley as a primary reference in the present rejection under 35 U.S.C. § 103(a) is the effect of Hartley as prior art to the present application under 35 U.S.C. § 102(e), since no other subsection of 35 U.S.C. § 102 apparently would apply. Applicants wish to remind the Examiner that, effective November 29, 1999, 35 U.S.C. § 103(c) has been amended such that:

subject matter developed by another person, which qualifies as prior art only under subsection (e), (f), and or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

American Inventors Protection Act of 1999 § 4807, 35 U.S.C. § 103(c) (Pub. L. 106-113, November 29, 1999). As noted above, the apparent basis for using Hartley in this rejection is its possible qualification as prior art only under 35 U.S.C. § 102(e), and Hartley and the present application were, at the time the present invention was made, owned by the same assignee or at least subject to an obligation of assignment to the same assignee. Applicants therefore respectfully assert that since the present Continued Prosecution Application was filed on August 22, 2000, *i.e.*, after the effective date of the amendment to 35 U.S.C. § 103(c), Hartley cannot be used as prior art in rejecting the presently claimed invention. Hence, Applicants respectfully

assert that any rejection or portion thereof that might be based on the disclosure of Hartley is in error.

With regards to the remaining primary references (Kilby and Snaith), Applicants respectfully assert that these references are seriously deficient and do not support a *prima facie* case of obviousness of the invention as presently claimed. As the Examiner has acknowledged (see Paper No. 8, page 5, third full paragraph), neither Kilby nor Snaith discloses adding recombination sites to nucleic acid molecules using a primer-based amplification method such as that of the presently claimed invention. The remaining references do not cure these deficiencies, since Ausubel, Padgett and Grose similarly do not disclose, suggest, or otherwise contemplate the addition of recombination sites to nucleic acid molecules using primers comprising such recombination site(s).

In proceedings before the Patent and Trademark Office, the examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. *See In re Piasecki*, 223 USPQ 785, 787-88 (Fed. Cir. 1984). The Examiner can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references in such a way as to produce the invention as claimed. *See In re Fine*, 5 USPQ2d 1596,1598 (Fed. Cir. 1988). Specifically, there must be a reason, suggestion, or motivation in the cited art that would motivate one of ordinary skill to combine the references, and that would also suggest a reasonable likelihood of success in making or using the invention as claimed as a result of that combination. *See In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988). In the present case, this burden has not been met. As noted above, Kilby and Snaith are seriously deficient as primary references (and Hartley is not available as prior art), while Ausubel, Padgett and Grose do not cure these deficiencies. Moreover, none of these references provides any reason,

suggestion or motivation that would lead one of ordinary skill to combine their disclosures to result in the presently claimed methods. The Examiner's attempt to analogize the introduction of recombination sites into nucleic acid molecules, to methods for introducing restriction sites (in Ausubel), enzyme recognition sites (in Padgett), or a peptide tag sequence (in Grose) is impermissible, since there is no suggestion or motivation in any of these references that one of ordinary skill should or could use such techniques to introduce recombination sites into nucleic acid molecules. Absent such suggestion and motivation, the cited references may not be properly combined to render the claimed invention obvious. *See Fine* at 1598. Moreover, there is no basis for concluding that an invention would have been obvious solely because it is a combination of elements that were known in the art at the time the invention was made, *see Fromson v. Advance Offset Plate, Inc.*, 755 F.2d 1549, 1556 (Fed. Cir. 1995), if there is no reason, suggestion, or motivation present in the prior art that would motivate one of ordinary skill to combine the cited references and have a reasonable expectation of success in making and using the claimed invention. *See In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988). Finally, even if these references *could* be properly combined (which they cannot), one of ordinary skill would have no reasonable expectation of success in making or using the presently claimed methods, since none of these references discloses or suggests the introduction of recombination sites encompassed by claim 26 as currently presented. Thus, Applicants respectfully assert that a *prima facie* case of obviousness cannot be established based on the combined disclosures of the cited references.

VI. The Rejection Under 35 U.S.C. § 112, Second Paragraph

In the Office Action at page 3, fourth paragraph, the Examiner has maintained the rejection of claim 30 under 35 U.S.C. § 112, second paragraph, for reasons set forth in Paper No. 8. Specifically, in making this rejection, the Examiner contended that:

[i]t is not clear what the distinction is between mRNA and poly A RNA; it appears that the recitation "poly A RNA" is redundant.

Paper No. 8 at page 8, fourth paragraph. Applicants respectfully disagree with this contention. As one of ordinary skill would appreciate, mRNA is only one type of polyadenylated (*i.e.*, polyA) RNA. In fact, RNA molecules can be polyadenylated synthetically (*e.g.*, via chemical synthesis, PCR, etc.) in ways that do not involve the production of mRNA molecules. Hence, Applicants respectfully assert that the term "polyA RNA" is not redundant with the term "mRNA" -- the latter is an example of or a species of the former. However, to expedite prosecution, Applicants have deleted the recitation "mRNA" from claim 30 and have introduced it into new claim 98 that is sought to be entered by the foregoing amendments. As noted above, these amendments are fully supported in the specification as originally filed, and therefore add no new matter. Accordingly, Applicants respectfully assert that claim 30 as currently presented is in full compliance with the clarity requirements of 35 U.S.C. § 112, second paragraph.

VII. Conclusion

It is believed that the present Continued Prosecution Application is in condition for immediate examination, and that the objections and rejections contained in the Office Action dated May 22, 2000, have been overcome by the foregoing remarks. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

HARTLEY *et al.*
Appl. No.: 09/177,387

- 12 -

Prompt entry and favorable consideration of the foregoing amendments and remarks are
earnestly solicited.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Brian J. Del Buono
Agent for Applicants
Registration No. 42,473

Date: October 27, 2000

1100 New York Avenue, N.W.
Suite 600
Washington, D.C. 20005-3934
(202) 371-2600